

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/25958

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
TPC(T) : C08K 3/04; C08F 293/00; C08L 53/00; GOIN 33/20; A61K 38/43		
US CL : 523/323, 299, 90; 436/73, 86; 424/94.1		
According to International Patent Classification (TPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) U.S. : 523/323, 299, 90; 436/73, 86; 424/94.1		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CAPLUS, BIOSIS, MEDLINE, WPIDS		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,087,452 A (STEWART et al.) 11 July 2000 (11.07.2000), column 3, line 5, through column 12, line 64.	1-44
Y	BROWN, K.C. et al. Determining protein-protein interactions by oxidative cross-linking of a glycine-glycine-histidine fusion protein Biochemistry. 1998, Vol. 367, pages 4397-4406, especially pages 4398-4399.	1-44
Y	US 6,077,371 A (LUNDSTROM et al) 20 June 2000 (20.06.2000), column 4, lines 50-56.	6
Y	MICHON, T. et al. Horseradish peroxidase oxidation of tyrosine-containing peptides and their subsequent polymerization: A kinetic study. Biochemistry. 1997, Vol. 36, pages 8504-8513, especially pages 8507-8510.	3-5
Y	FANCY, D.A. et al. A critical role for tyrosine residues in Ni <sup>2+</sup> -mediated protein cross-linking Biochem Biophys. Res. Comm. 1998, Vol. 247, page 420-426, especially page 422	1-44
<input type="checkbox"/> Further documents are listed in the continuation of Box C <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents	T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	
"B" earlier application or patent published on or after the international filing date	"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family	
"O" document referring to an oral disclosure, use, exhibition or other means		
T" document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search	Date of mailing of the international search report/ <b>15 NOV 2005</b>	
13 October 2005 (13.10.2005)		
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Lora E. Barnhart Telephone No. 571-272-1600	

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Box No.  $\pi$  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. HI Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-44

- Remark on Protest
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
  - ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
  - ☐ No protest accompanied the payment of additional search fees.

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### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACIONG

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-44, drawn to a method of crosslinking two moieties.

Group II, claim(s) 45-53, drawn to a method of crosslinking two proteins.

Group III, claim(s) 54-63, drawn to a method of conjugating a protein to a synthetic polymer.

Group IV, claim(s) 64-69, drawn to a method of immobilizing a protein on a polymer surface.

Group V, claim(s) 70-79, drawn to a material made by crosslinking a polymer.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: They lack inventive unity a priori. The Groups are drawn to four distinct methods and a product that is not used by or made by any of said methods. Group I requires attaching metal ions to two moieties; Group II requires attaching HY-tags to two proteins; Group III requires attaching a metal-binding peptide to a protein and a ligand to a polymer; Group IV requires attaching a metal-binding peptide to a protein and somehow modifying a surface. None of these methods share starting products, process steps, or end points, and none of them result in or require the product of Group V, which is a composition comprising a polymer cross-linked to a metal. Because the Groups have no material common to all of them, they lack inventive unity a priori.